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Comparison of the Responses of Children and Adults to Acute Ozone Exposure

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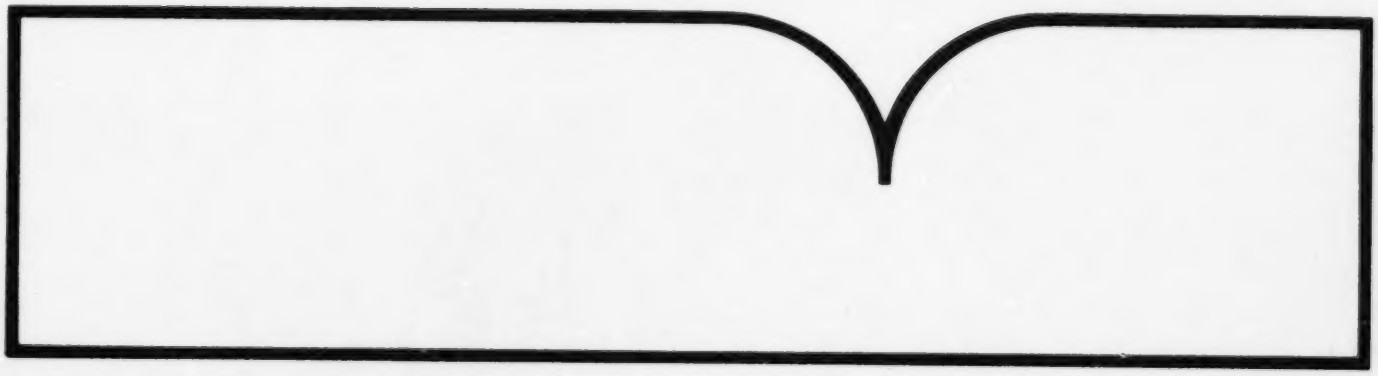

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16. ABSTRACT

The purpose of this paper is to compare the results of two studies in which the respiratory responses of children and adults to acute ozone (O_3) exposure were measured. Forty-two 18-30 year old males were exposed for 2.5 hours in a controlled environmental chamber to either 0.0 or 0.12 ppm O_3 while performing intermittent heavy exercise. Twenty-two 8-11 year old males were exposed in a similar manner to both air and 0.12 ppm O_3. Measures of respiratory symptoms and function were made before and after exposure. Adults experienced an increase in the symptom cough and decrements in forced vital capacity and some measures of forced expiratory flow. Children experienced similar decrements in pulmonary function, but had no increase in symptoms. We concluded that as measured by pulmonary function children appear to be no more responsive to O_3 exposure than are adults and may experience fewer symptoms.

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A COMPARISON OF THE RESPONSES OF CHILDREN AND ADULTS TO ACUTE OZONE EXPOSURE

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The purpose of this paper is to compare the results of two studies in which the respiratory responses of children and adults to acute ozone (O_3) exposure were measured. Forty-two 18-30 year old males were exposed for 2.5 hours in a controlled environmental chamber to either 0.0 or 0.12 ppm O_3 while performing intermittent heavy exercise. Twenty-two 8-11 year old males were exposed in a similar manner to both air and 0.12 ppm O_3. Measures of respiratory symptoms and function were made before and after exposure. Adults experienced an increase in the symptom cough and decrements in forced vital capacity and some measures of forced expiratory flow. Children experienced similar decrements in pulmonary function, but had no increase in symptoms. We concluded that with exercise normalized for body size, children appear to be no more responsive to O_3 exposure as measured by pulmonary function than are adults and may experience fewer symptoms.

INTRODUCTION

Epidemiologic studies have suggested that children exposed to ambient levels of ozone (O_3) below 0.12 ppm (the National Ambient Air Quality Standard) experience changes in respiratory function (1,2,3,4). We have previously demonstrated that the exposure of heavily exercising adults to 0.12 ppm O_3 in a controlled chamber environment results in the onset of symptoms and in decrements in pulmonary function (5). Adults exposed to 0.10 ppm O_3, however, were not found to have changes in respiratory function (6). It has not been possible to answer the question of whether children are more responsive to O_3 exposure than are adults because studies have not been performed on both groups under comparable conditions. The purpose of this paper is to compare the results of a previous study of adults exposed to 0.12 ppm O_3 with those of a similar study of children.

MATERIALS AND METHODS

Subjects for the study of adults were 18-30 years old, and for the study of children were 8-11 years of age. All subjects were healthy nonsmoking White males without a history of asthma, allergic rhinitis, chronic respiratory disease, or recent acute respiratory illness. All subjects were interviewed and examined by a physician, and hematologic and serum chemical screens were performed prior to any exposure. The purposes, procedures and potential risks of the study were explained to the accepted subjects (and parents, in the case of children), and each signed a consent form. These studies were approved by the Committee for the Protection of the Rights of Human Subjects of the University of North Carolina School of Medicine.

Forty-two adult subjects were studied between September 1980 and June 1981. Twenty were exposed to clean air, and twenty-two were exposed to 0.12 ppm O_3. These forty - two subjects were part of a larger group of 135 subjects each exposed to one of six different levels of O_3. Twenty-two children were exposed to both clean air and to 0.12 ppm O_3 with the two exposures separated by at least one week. They were exposed between June and August 1983.

Prior to exposure, each subject underwent a training session during which time he learned to perform spirometric and plethysmographic measurements. Each subject also exercised on a treadmill, and the speed and grade of incline required to produce a minute ventilation ($\dot{V}_E$) of 35 l/min/m^2BSA were determined.

The exposures for both studies were performed in the following manner. Prior to exposure, subjects performed measurements of airways resistance

and thoracic gas volume in a standard variable-pressure body plethysmograph (CPI model 2000TR) from which specific airways resistance (SRaw) was calculated. Subjects also performed forced vital capacity (FVC) maneuvers on a 12 l dry-seal spirometer (CPI model 220) from which measures of FVC, forced expiratory volume in 1 second (FEV_1), forced expiratory flow rate between 25% and 75% of FVC (FEF_{25-75}), and peak expiratory flow rate (PEF) were determined. The flow-volume curve for each maneuver was examined for technical problems or poor performance. Subjects then entered the chamber with the appropriate O_3 concentration, and immediately answered a symptom questionnaire regarding the presence and severity of cough, shortness of breath, and pain upon deep inspiration. Each symptom was reported as "none", "mild", "moderate", "severe" with scores of 1, 2, 3, or 4 assigned, respectively. The exposure period was for 2.5 hours, the first 2 hours consisting of alternating 15 minute periods of rest and heavy treadmill exercise at the speed and grade of incline determined during the training session. During the 11th and 12th minutes of each exercise period, measurements of $\dot{V}_E$, respiratory frequency (f), and tidal volume (V_T) were made by integration of flow signals from a Fleisch no. 3 pneumotachometer. Heart rate (HR) was measured by single lead ECG telemetry. Final measurements of spirometric and symptom variables were performed five and ten minutes, respectively, following the last exercise period. Twenty-five minutes following the last exercise, final plethysmographic measures were made.

Exposure and measurements were conducted in a 4 x 6 x 3.2-m stainless steel chamber maintained at 22°C and 40% relative humidity. Ozone was generated by passing incoming air over ultraviolet lights. The concentration of O_3 in the chamber was continuously monitored by chemiluminescence

detection using Bendix model 8002 analyzers, which were periodically calibrated against an ultraviolet O_3 photometer (Dasibi model 1003AH). A detailed description of the chamber and the O_3-generating, delivery, monitoring, and control systems has been previously published (7,8).

For the spirometric, plethysmographic, and symptom variables, the differences between the initial and final measurements were calculated and analyzed. For measures of f and V_T, differences between the first and fourth exercise periods were calculated. For measures of $\dot{V}_E$ and HR, which characterize the response to exercise, and for measures of treadmill speed and elevation, values for all four exercise sessions were averaged for each subject. In the study of children, differences between the air and O_3 exposures were tested for by the paired student's t-test since each subject was exposed to both air and O_3. In the study of adults, differences between the air group and the 0.12 ppm O_3 group were tested for by the nonparametric Williams test. This test was used because in the adult study the results of the air group were also tested against the results of four other groups, each exposed to a concentration of O_3 different from 0.12 ppm. Statistical comparisons of the O_3 effects between children and adults were not performed due to the repeated measures design in the children study and the use of independent samples in the adult study.

For the study of adults, nine hypotheses were formally tested. These were for differences between the air and O_3 exposures for FVC, FEV_1, FEF_{25-75}, SRaw, f, V_T, cough, shortness of breath, and pain on deep inspiration. Because multiple hypotheses were tested, some adjustment of p values may be necessary. However, because most of these variables are correlated with each other the adjustment is small. The analysis for PEF was performed

as a hypothesis generating analysis. For the study of children, two formal hypotheses were tested: for differences between the air and O_3 exposures for changes in FEV_1 and cough. Analyses of other variables are reported and were performed as hypothesis generating analyses.

RESULTS

The baseline lung function values were within normal limits for all adults and children and were similar on both exposure days (Table 1). The exercise load and response to exercise were similar on both exposure days for children and for adults (Table 2). As expected, the $\dot{V}_E$ for adults was greater than for children. However, the $\dot{V}_E$ normalized for BSA was similar for the adults and children, as was HR.

Following the air exposure of adults small average decreases in FVC and forced expiratory flows were observed. Larger decreases were observed following O_3 exposure (Table 3). For children, percent decreases in pulmonary function following air exposure were small and similar to those for adults with the exception of PEF which was increased slightly in children. Following O_3 exposure, children had larger decreases than following air exposure in each of the variables measured. The magnitudes of the percent decreases were similar to those observed in adults. There were no significant changes in SRaw, f, V_T, shortness of breath, or pain on deep inspiration following O_3 exposure compared to the air exposure for either children or adults.

Exposure to O_3 resulted in a large increase in the symptom cough reported by adults. Children, however, experienced little or no increase in cough following O_3 exposure. Neither group experienced changes in cough following clean air.

DISCUSSION

The results of these studies indicate that heavily exercising children and adults experience small but significant decrements in FEV_1 when exposed to 0.12 ppm O_3 for 2 hours. In addition, since the underlying mechanisms limiting FEV_1 are probably the same as those limiting FVC and other forced expiratory flows, it is likely that the decreases in PEF measured in adults and the decreases in FVC and FEF_{25-75} measured in children represent real differences from the air exposure. These observations are consistent with those of Lippmann et al (4) who reported decreases in FVC and FEV_1 when children were exposed to 0.11 ppm O_3 compared to days with lower concentrations. Similarly, Lebowitz and associates (1) observed an inverse relationship between ambient ozone concentrations and PEF when children and adolescents exercised under ambient conditions. Chamber studies comparable to these two studies have been performed at 0.08, 0.10, and 0.16 ppm O_3 for adults, but not at 0.12 ppm. Folinsbee et al (6) observed no changes in respiratory function in 8 adult males exposed to 0.10 ppm O_3 while performing heavy intermittent exercise for 2 hours. In a study of bicyclists performing moderately heavy continuous exercise for 1 hour, Avol and associates (9) measured no change in FVC or FEV_1 following exposure to 0.08 ppm O_3 compared to control, but did measure changes in these variables at 0.16 ppm O_3 that were larger than the changes measured in this study.

Determination of the relative sensitivity or responsiveness of different groups to O_3 exposure requires comparable measures of response and comparable exposures. In this report we have presented percent decreases rather than absolute decreases in spirometric measurements as the measure of response

because adults can experience much larger absolute decreases in FVC and forced expiratory flows than can children. We believe that expressing decrements as a percent of baseline allows more valid comparison of findings in the two groups than would comparison of absolute changes.

The determinants of response to O_3 exposure include concentration, $\dot{V}_E$ during exposure, and duration of exposure (6). In our studies the concentration, duration, and exposure protocol were identical for children and adults. The target $\dot{V}_E$'s for the two groups were not set to be equal because children cannot generally attain the $\dot{V}_E$ of adults. Since it is clear that some normalization must occur, we normalized $\dot{V}_E$ according to body surface area, and we achieved levels of exercise resulting in heart rate and normalized $\dot{V}_E$ for the children within approximately 7% of that of adults. There are other characteristics upon which $\dot{V}_E$ can be normalized; however, there is no empirical evidence demonstrating that one function of $\dot{V}_E$ is better than another in predicting changes in lung function. Likewise, we are not able on theoretical grounds to choose the single most appropriate method of normalization because the mechanisms of O_3 response have not been elucidated.

Having used what we believe are appropriate measures of response and comparable exposures, we observed that for the spirometric variables, the effects due to O_3 exposure (i.e. responses to O_3 minus the responses to air) were very similar for both adults and children. On the other hand, adults clearly had an increase in cough as a result of exposure, whereas children had no increase. The reason for this difference is not clear. One possible explanation is that the mechanisms responsible for these two effects are different and that children and adults differ in their ability

to have these mechanisms stimulated by O_3 exposure. Another possibility is that children are less likely to report symptoms than adults. Though we cannot rule out this possibility, at least one investigator was with the exposed child at all times and with rare exceptions no coughing was observed.

In summary, we conclude that during heavy intermittent exercise, both adults and children exposed for two hours to 0.12 ppm O_3 experience small decrements in pulmonary function. For levels of exercise producing comparable ventilations normalized for BSA, there appears to be no difference between the response of children and adults. Adults also experienced an increase in the symptom cough during these exposures. Children had no increase in cough and appear to be less responsive to O_3 regarding the induction of the symptom cough.

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Table 1

Baseline Lung Function Values and Demographic Measurements For Children and Adults

	Children		Adults	
	Air	Ozone	Air	Ozone
FVC (l)	2.35	2.34	5.34	5.61
FEV_1 (l)	1.97	1.98	4.42	4.64
FEF_{25-75} (l/sec)	2.13	2.18	4.51	4.87
PEF (l/sec)	4.43	4.58	10.76	10.36
SRaw (cm/sec)	4.64	4.58	4.50	4.34
Age (yrs)	9.9	9.9	22.5	22.3
Height (cm)	141	141	180	183

Table 2

Exercise Levels and Response to Exercise

	Children		Adults	
	Air	Ozone	Air	Ozone
TRSP (km/hr)	4.6 ± 0.3	4.6 ± 0.3	5.7 ± 0.2	5.8 ± 0.2
TREL (%)	15.0 ± 0.0	15.0 ± 0.0	11.3 ± 1.3	11.8 ± 1.6
HR (beats/min)	158 ± 13	158 ± 15	166 ± 10	163 ± 12
$\dot{V}_E$ (l/min)	38.2 ± 6.2	39.4 ± 7.4	66.2 ± 7.6	68.0 ± 7.4
$\dot{V}_E/BSA$ ($l/min/m^2$)	32.4 ± 3.3	33.3 ± 3.4	34.9 ± 3.1	34.3 ± 2.9

Values are means ± S.D.

TRSP = Treadmill speed, TREL = treadmill elevation, HR = heart rate, $\dot{V}E$ = minute ventilation, BSA = Body surface area.

Table 3

Changes In Respiratory Function From Baseline Following Exposure To Air or 0.12 ppm Ozone

	Children*			Adults		
	Air	Ozone	p	Air†	Ozone*	p
FVC (%)	-0.1 ±0.7	-1.8 ±0.7	.08	-0.9 ±0.4	-3.1 ±1.1	.04
FEV_1 (%)	-0.5 ±1.1	-3.4 ±1.1	.03	-1.1 ±0.5	-4.3 ±1.1	.02
FEF_{25-75} (%)	-2.2 ±2.2	-5.3 ±2.5	.19	-0.4 ±1.5	-7.2 ±2.2	.03
PEF (%)	+2.1 ±2.0	-2.7 ±1.9	.05	-2.9 ±1.7	-3.9 ±2.4	>.05
Cough	0.0+ ±0.1	0.1+ ±0.2	.16	0.1§ ±0.0	0.8** ±0.2	<.005

*n = 22

+n = 23

†n = 20

§n = 17

**n= 21

Cough was scored before and after exposure as none = 1, mild = 2, moderate = 3, severe = 4. Changes are reported as the absolute differences of these measures.

Values for other variables are differences expressed as a percent of baseline.

Measures of variability are S.E.

P-values for children are calculated by a paired t test

P-values for adults are calculated by the nonparametric Williams' test

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